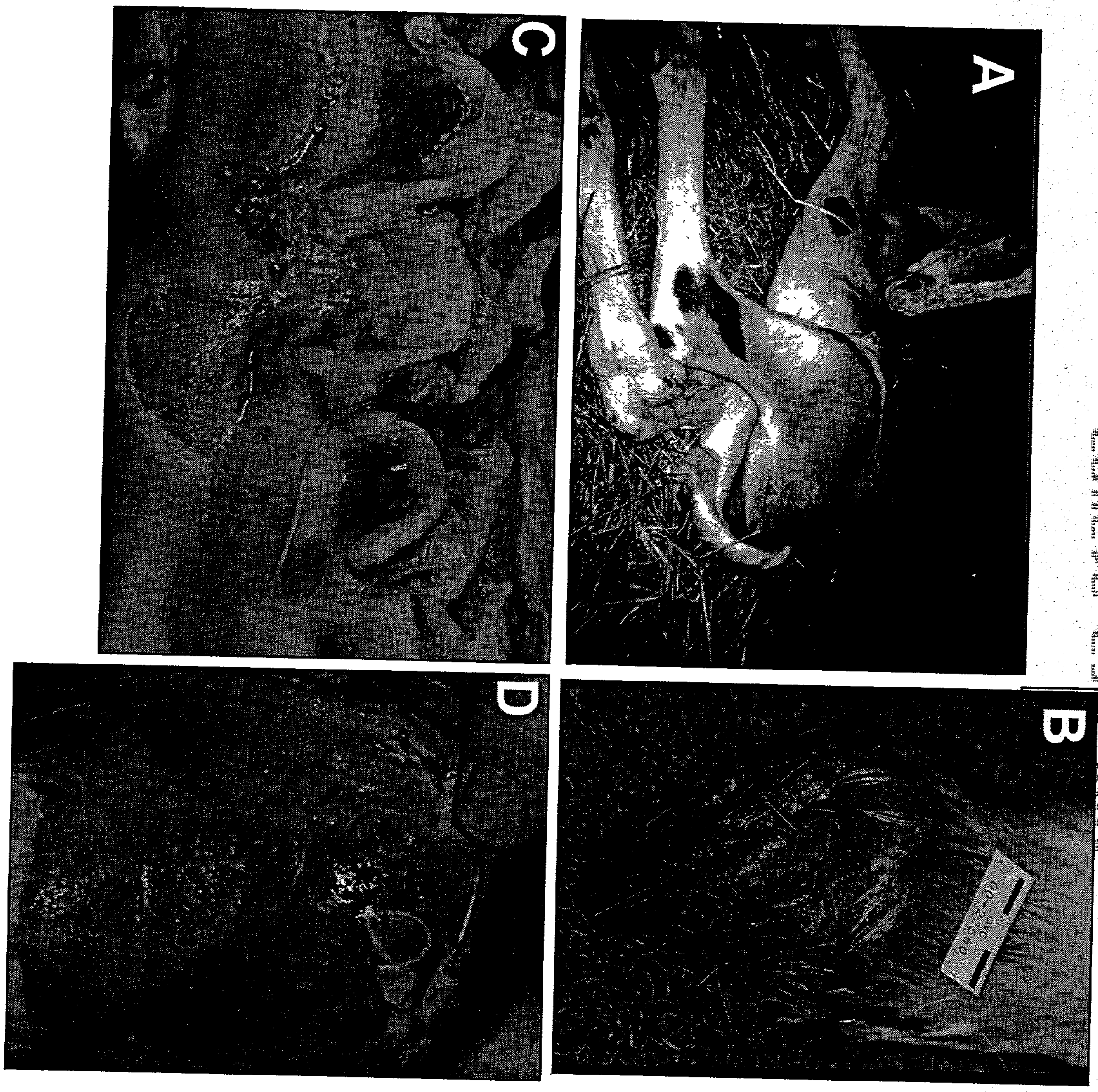

FIG. 1

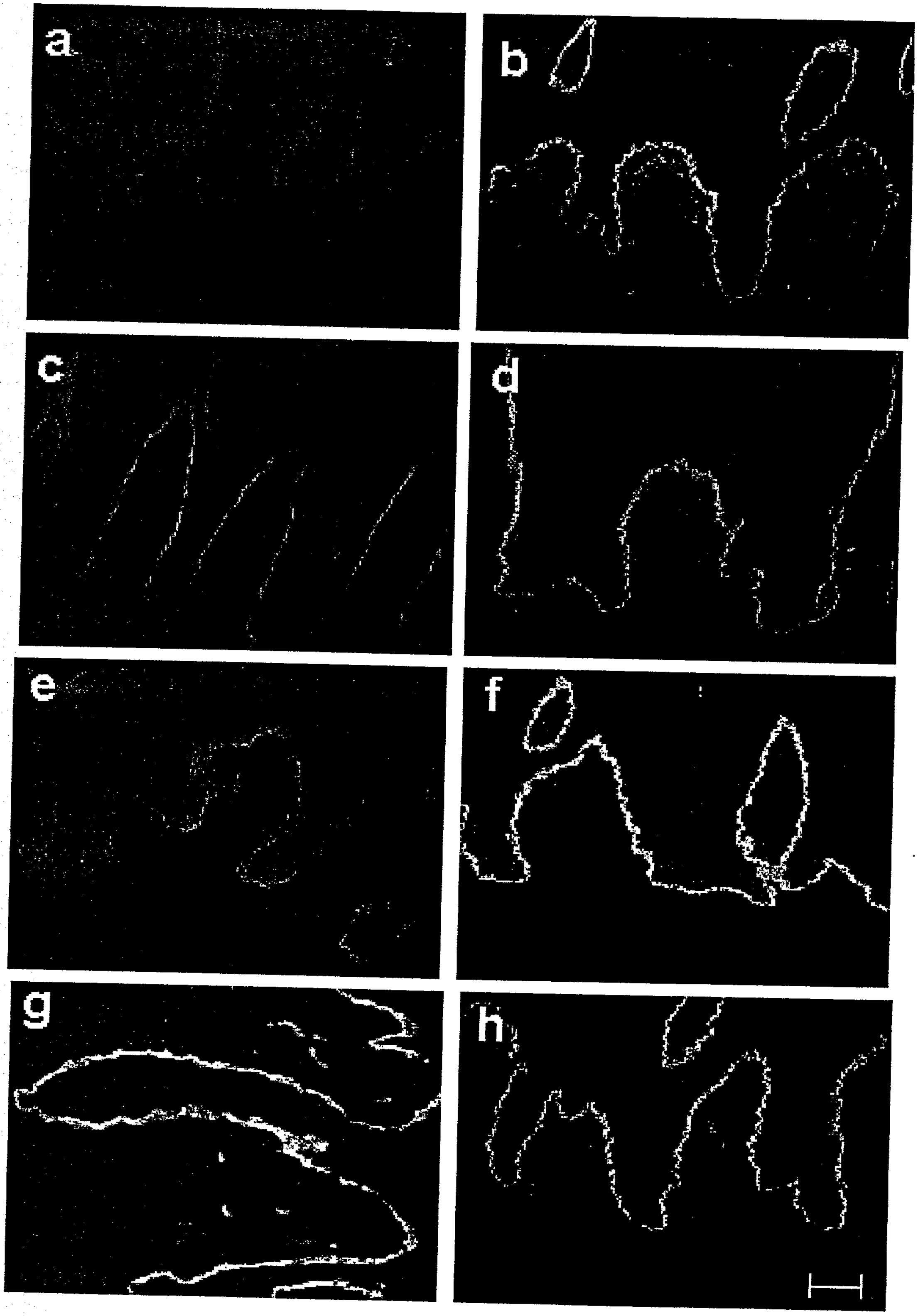

FIG. 2

```
                                                                      5'TGGGTCCTCCTTATTCACAGG    -177
TGAGTCACACCCTGAAACACAGGCTCTCTTCCTGTCAGGACTGAGTCAGGTAGAAGAGTCGATAAAACCACCTGATCAGGAAAAG      -91
GAAGGCACAGCGGAGCGCAGAGTGAGAACTCCCAGCGGCGAGGCGCCGGGCAGCGACCCCTGCAGCGGCGGACCGCGCGCCGGCCTGGCC -1

ATGCCTGCGCTCTGGCTGAGCTGCTACCTCTGCTTCTCGCTCCTCCTGCCCGCAGCCCGGGCCACCTCCGGGAGGGAAGTCTGTGATTGC 90
M  P  A  L  W  L  S  C  Y  L  C  F  S  L  L  L  P  A  A  R  A  T  S  G  R  E  V  C  D  C   30
                                                        ↑                 |——▶      Dom V
AACGGGAAGTCCAGGCAATGCATCTTTGACCAGGAACTTCACAAACAGACAGGAAATGGATTCCGCTGCCTCAACTGCAATGACAACACT 180
N  G  K  S  R  Q  C  I  F  D  Q  E  L  H  K  Q  T  G  N  G  F  R  C  L  N  C  N  D  N  T   60

GATGGCATCCACTGCGAGAGGTGCAAGGCAGGATTTTACCGACAGAGAGAAAGGGACCGCTGTTTACCCTGCAATTGTAACTCTAAAGGT 270
D  G  I  H  C  E  R  C  K  A  G  F  Y  R  Q  R  E  R  D  R  C  L  P  C  N  C  N  S  K  G   90

TCTCTTAGCGCTCGATGTGACAACTCTGGACGGTGCAGCTGTAAGCCAGGTGTGACAGGAGACAGGTGTGACCGATGTCTGCCCGGCTTC 360
S  L  S  A  R  C  D  N  S  G  R  C  S  C  K  P  G  V  T  G  D  R  C  D  R  C  L  P  G  F   120

CACACACTCACTGATGCTGGGTGCGCCCAAGACCAAAGGCTGCTAGACTCCAAGTGTGACTGTGACCCAGCTGGCATCTCAGGGCCCTGT 450
H  T  L  T  D  A  G  C  A  Q  D  Q  R  L  L  D  S  K  C  D  C  D  P  A  G  I  S  G  P  C   150

GACTCAGGCCGCTGTGTCTGCAAGCCGGCTGTCACTGGAGAGCGCTGTGATAGGTGTCGACCAGGTTACTATCACCTGGATGGGGGAAAC 540
D  S  G  R  C  V  C  K  P  A  V  T  G  E  R  C  D  R  C  R  P  G  Y  Y  H  L  D  G  G  N   180

CCTCAGGGCTGTACCCAGTGTTTTTGCTATGGGCATTCCGCCAGCTGCCACAGCTCTGGGGACTACAGTGTCCATAAAATCATCTCTGCC 630
P  Q  G  C  T  Q  C  F  C  Y  G  H  S  A |S  C  H  S  S  G  D  Y  S  V  H  K  I  I  S  A   210
                                          |——▶     dom. IV
TTCCATCAAGATGTTGATGGCTGGAAGGCTGTCCAAAGAAACGGGTCTCCTGCAAAGCTCCAGTGGTCACAGCGCCATCGGGATATATTT 720
F  H  Q  D  V  D  G  W  K  A  V  Q  R [N  G  S] P  A  K  L  Q  W  S  Q  R  H  R  D  I  F   240

AGCTCAGCACGACGATCAGACCCTGTCTATTTTGTAGCTCCTGCCAAATTTCTTGGGAATCAACAGGTGAGCTACGGGCAAAGCCTATCT 810
S  S  A  R  R  S  D  P  V  Y  F  V  A  P  A  K  F  L  G  N  Q  Q  V  S  Y  G  Q  S  L  S   270

TTTGACTACCGTGTGGATAGGGGAGGCAGACACCCATCTGCCCATGACGTGATCCTGGAAGGTGCTGGTCTACGGATCACAGCTCCCTTG 900
F  D  Y  R  V  D  R  G  G  R  H  P  S  A  H  D  V  I  L  E  G  A  G  L  R  I  T  A  P  L   300

ATGCCACTTAGCAAGACACTGCCTTGTGGGATCACCAAGACTTACACATTCAGATTAAATGAACATCCAAGCAGTAATTGGAGCCCCCAG 990
M  P  L  S  K  T  L  P  C  G  I  T  K  T  Y  T  F  R  L  N  E  H  P  S  S [N  W  S] P  Q   330

CTAAGTTACTTTGAGTATCGGAGGTTACTGCGGAACCTCACAGCCCTGCGGATCCGAGCTACCTACGGAGAATACAGTACTGGGTACATT 1080
L  S  Y  F  E  Y  R  R  L  L  R [N  L  T] A  L  R  I  R  A  T  Y  G  E  Y  S  T  G  Y  I   360

GACAACGTGACCTTGATTTCAGCCCGCCCCGTTTCTGGAGCCCCAGCGCCCTGGGTTGAACAATGTGTATGCCCTGTTGGCTACAAGGGG 1170
D [N  V  T] L  I  S  A  R  P  V  S  G  A  P  A  P  W  V  E |Q  C  V  C  P  V  G  Y  K  G   390
                                                           |——▶        Dom. III
CAGTTCTGCCAGGATTGTGCTTCCGGCTACAAAAGAGATTCAGCCAGACTGGGACCTTTTGGCACCTGTATTCCATGTAACTGCCAAGGG 1260
Q  F  C  Q  D  C  A  S  G  Y  K  R  D  S  A  R  L  G  P  F  G  T  C  I  P  C  N  C  Q  G   420

GGAGGGGCCTGCGATCCAGACACAGGAGACTGTTACTCAGGGGATGAGAACCCTGACATCCCTGAGTGTGCTGACTGCCCCATTGGTTTC 1350
G  G  A  C  D  P  D  T  G  D  C  Y  S  G  D  E  N  P  D  I  P  E  C  A  D  C  P  I  G  F   450

TACAACGATCCACAAGACCCCCGCAGCTGCAAGCCGTGCCCCTGTCGCAATGGGTTCAGCTGCTCCGTGATGCCTGAGACAGAGGAGGTG 1440
Y  N  D  P  Q  D  P  R  S  C  K  P  C  P  C  R  N  G  F  S  C  S  V  M  P  E  T  E  E  V   480

GTGTGCAATAACTGCCCCCAGGGTGTCACTGGTGCCCGCTGTGAGCTCTGTGCTGATGGCTATTTTGGGGACCCCTTCGGGGAACGTGGC 1530
V  C  N  N  C  P  Q  G  V  T  G  A  R  C  E  L  C  A  D  G  Y  F  G  D  P  F  G  E  R  G   510

CCAGTGAGGCCTTGTCAGCCCTGTCAGTGCAACAACAACGTGGACCCTAGTGCCTCCGGGAACTGTGACCGCCTGACAGGCAGGTGTCTG 1620
P  V  R  P  C  Q  P  C  Q  C  N  N  N  V  D  P  S  A  S  G  N  C  D  R  L  T  G  R  C  L   540

AAGTGCATCCACAACACAGCTGGGGTCCACTGTGACCAGTGCAAAGCAGGCTACTATGGGGACCCGTTGGCTCCCAATCCAGCAGACAAG 1710
K  C  I  H  N  T  A  G  V  H  C  D  Q  C  K  A  G  Y  Y  G  D  P  L  A  P  N  P  A  D  K   570

TGTCGAGCTTGCAACTGCAACCCAGTGGGCTCGGAGCCTGTGGAGTGTCGAAGTGATGGCAGCTGTGTTTGCAAGCCAGGCTTTGGTGGC 1800
C  R  A  C  N  C  N  P  V  G  S  E  P  V  E  C  R  S  D  G  S  C  V  C  K  P  G  F  G  G   600
```

FIG. 3

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CTCAGCTGTGAGCATGCGGCACTGACCAGCTGTCCAGCTTGCTATAATCAAGTGAAGGTTCAGATGGATCAGTTTATGCAGCAGCTCCAG 1890
L  S  C  E  H  A  A  L  T  S  C  P  A  C  Y  N  Q  V  K  V  Q  M  D  Q  F  M  Q  Q  L  Q   630
                        Dom. I/II
ATCCTGGAGGCCCTGATTTCGAAGGCTCAGGGTGGAGCAGTACCCAACGCAGAGCTGGAAGGCAGGATGCAGCAGGCTGAGCAGGCCCTT 1980
I  L  E  A  L  I  S  K  A  Q  G  G  A  V  P  N  A  E  L  E  G  R  M  Q  Q  A  E  Q  A  L   660

CGGGACATTCTGAGAGAAGCCCAGATTTCACAAGATGCTGTTAGATCCTTCAATCTCCGGGTGGCCAAGGCAAGGACTCAAGAGAATAGC 2070
R  D  I  L  R  E  A  Q  I  S  Q  D  A  V  R  S  F  N  L  R  V  A  K  A  R  T  Q  E  N  S   690

TACCGGGACCGCCTGGATGACCTCAAGATGACTGTGGAAAGAGTTCGGGCCCTGGGCAGTCAGTATCAGAACCAAGTTCAGGATACTCGC 2160
Y  R  D  R  L  D  D  L  K  M  T  V  E  R  V  R  A  L  G  S  Q  Y  Q  N  Q  V  Q  D  T  R   730

AGGCTCATCACTCAGATGCGCCTGAGCCTGGAGGAAAGTGAGGCTTCCCTGCAAAACACCAACATTCCTCCTTCAGAGCACTACGTGGGG 2250
R  L  I  T  Q  M  R  L  S  L  E  E  S  E  A  S  L  Q  N  T  N  I  P  P  S  E  H  Y  V  G   750

CCAAATGGCTTTAAAAGTCTGGCTCAGGAGGCCACGAGATTGGCAGACAGCCATGTTCAGTCAGCCAGTAACATGGAGCAACTGGCAAAG 2340
P  N  G  F  K  S  L  A  Q  E  A  T  R  L  A  D  S  H  V  Q  S  A  S  N  M  E  Q  L  A  K   780

GAAACCCAGGAGTATTCCAAAGAGCTGATGTCACTGGTGCGCGAGGCTCTGCAGGAAGGAGGCGGAAGCGGCAGCCTGGACGGAGCCGTG 2430
E  T  Q  E  Y  S  K  E  L  M  S  L  V  R  E  A  L  Q  E  G  G  G  S  G  S  L  D  G  A  V   810

GTGCAAAGGCTTGTGGGAAAATTGCAGAAAACTAAATCTCTGGCCCAGGAGTTGTCGAGGGAGGCCACGCAAACCGACATGGAAGCAGAT 2520
V  Q  R  L  V  G  K  L  Q  K  T  K  S  L  A  Q  E  L  S  R  E  A  T  Q  T  D  M  E  A  D   840

AGGTCTTATCAGCATAGTCTCCACCTTCTCAATTCCGTGTCTCAGATTCAGGGAGTCAATGATCAGTCCTTGCAGGTAGAAGCGAAGAGG 2610
R  S  Y  Q  H  S  L  H  L  L  N  S  V  S  Q  I  Q  G  V  N  D  Q  S  L  Q  V  E  A  K  R   870

CTCAGACAAAAAGCTGATTCTCTCTCAAACCGTGTGACTAAGCATATGGATGAGTTCAAGCACGTGCAAAGCAATCTGGGAAACTGGGAA 2700
L  R  Q  K  A  D  S  L  S  N  R  V  T  K  H  M  D  E  F  K  H  V  Q  S  N  L  G  N  W  E   900

GAAGAAACCCGGCAGCTCTTACAGAATGGAAAGAATGGGAGACAGACATCAGATCAGCTGCTTTCCCGTGCCAACCTTGCTAAAAGCAGA 2790
E  E  T  R  Q  L  L  Q  N  G  K  N  G  R  Q  T  S  D  Q  L  L  S  R  A  N  L  A  K  S  R   930

GCCCAAGAAGCACTAAGTATGGGCAATGCCACTTTTTATGAAGTTGAGAACATCTTAAAGAATCTCAGAGAGTTTGACCTGCAGGTTGGA 2880
A  Q  E  A  L  S  M  G  N  A  T  F  Y  E  V  E  N  I  L  K  N  L  R  E  F  D  L  Q  V  G   960

GATAAAAGAGCAGAAGCTGAAGAGGCCATGAAGAGACTCTCCTACATCAGCCAGAAGGTTGCAGGTGCCAGTGACAAGACGAAGCAAGCA 2970
D  K  R  A  E  A  E  E  A  M  K  R  L  S  Y  I  S  Q  K  V  A  G  A  S  D  K  T  K  Q  A   990

GAAGCAGCCCTGGGCAGTGCTGCTGCCGACGCCCAGAGGGCAAAGAATGCAGCCAGGGAGGCCCTGGAGATCTCTGGCAAGATAGAACAG 3060
E  A  A  L  G  S  A  A  A  D  A  Q  R  A  K  N  A  A  R  E  A  L  E  I  S  G  K  I  E  Q  1020

GAGATAGGAGGTCTGAACTTGGAAGCCAATGTGACAGCAGATGGAGCCTTGGCCATGGAGAAGGGACTGGCCACTCTGAAAAGTGAGATG 3150
E  I  G  G  L  N  L  E  A  N  V  T  A  D  G  A  L  A  M  E  K  G  L  A  T  L  K  S  E  M  1050

AGAGAAGTGGAAGGAGAGCTGTCAAGGAAGGAGCAGGAGTTTGACATGGATATGGACGCAGTGCAGATGGTAATTGCAGAGGCCCAAAGA 3240
R  E  V  E  G  E  L  S  R  K  E  Q  E  F  D  M  D  M  D  A  V  Q  M  V  I  A  E  A  Q  R  1080

GTTGAAAACAGAGCCAAGAATGCTGGAGTTACGATCCAAGACACACTCAACACATTGGATGGCATCCTACACCTAATAGACCAGCCTGGC 3330
V  E  N  R  A  K  N  A  G  V  T  I  Q  D  T  L  N  T  L  D  G  I  L  H  L  I  D  Q  P  G  1110

AGTGTGGATGAAGAGAGGCTGATCTTACTGGAGCAGAAGCTTTTCCGAGCCAAGACTCAGATCAACAGCCAGCTACGGCCCTTGATGTCA 3420
S  V  D  E  E  R  L  I  L  L  E  Q  K  L  F  R  A  K  T  Q  I  N  S  Q  L  R  P  L  M  S  1140

GAGCTGGAAGAGAGGGCACATCGGCAGAAGGGCCACCTCCGTTTCCTGGAGACTAGCATAGATGGGATTCTGGCTGATGTGAAGAACCTG 3510
E  L  E  E  R  A  H  R  Q  K  G  H  L  R  F  L  E  T  S  I  D  G  I  L  A  D  V  K  N  L  1170

GAGAACATCAGGGACAACCTGCCCCCGGGCTGCTACAATACCCAGGCTCTTGAGCAACAGtgaagctgccttagagatttctcaaccaag 3600
E  N  I  R  D  N  L  P  P  G  C  Y  N  T  Q  A  L  E  Q  Q  *                             1190
gttcttgggattcagacctagctgccttagagatttctcaaccaaggttcttgggattcagacctcagggctcaggagcccgcatgcggg 3690
tggggtgggatgggaatatttgaatatgttgaatgcgtgtgctcaggccccagtgaacctgatcccatccctgagacctcggccagataa 3780
atgtctttattg                                                                               3789-3'
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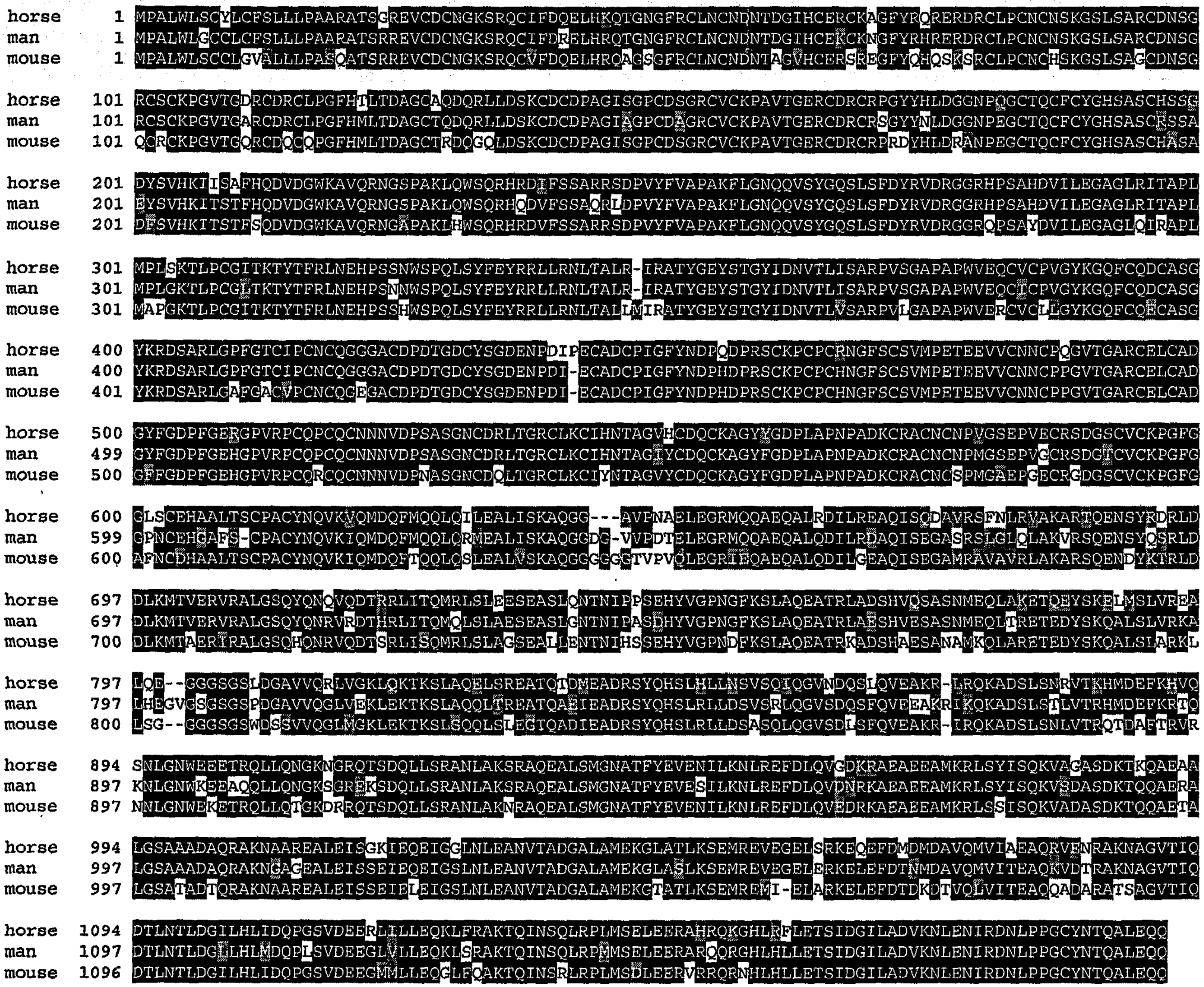
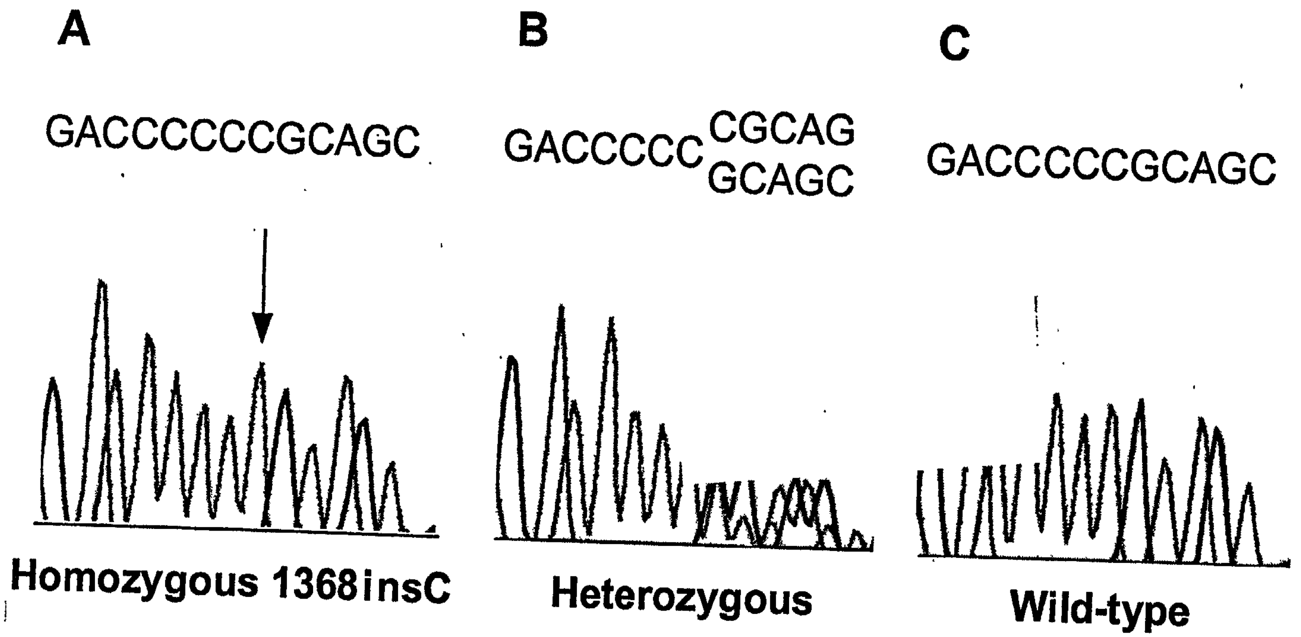
FIG. 3 cont'd



```
horse     1 MPALWLSCYLCFSLLLPAARATSGREVCDCNGKSRQCIFDQELHKQTGNGFRCLNCNDNTDGIHCERCKAGFYRQRERDRCLPCNCNSKGSLSARCDNSG
man       1 MPALWLGCCLCFSLLLPAARATSRREVCDCNGKSRQCIFDRELHRQTGNGFRCLNCNDNTDGIHCEKCKNGFYRHRERDRCLPCNCNSKGSLSARCDNSG
mouse     1 MPALWLSCCLGVALLLPASQATSRREVCDCNGKSRQCVFDQELHRQAGSGFRCLNCNDNTAGVHCERSREGFYQHQSKSRCLPCNCHSKGSLSAGCDNSG

horse   101 RCSCKPGVTGDRCDRCLPGFHTLTDAGCAQDQRLLDSKCDCDPAGISGPCDSGRCVCKPAVTGERCDRCRPGYYHLDGGNPQGCTQCFCYGHSASCHSSG
man     101 RCSCKPGVTGARCDRCLPGFHMLTDAGCTQDQRLLDSKCDCDPAGIAGPCDAGRCVCKPAVTGERCDRCRSGYYNLDGGNPEGCTQCFCYGHSASCRSSA
mouse   101 QCRCKPGVTGQRCDQCQPGFHMLTDAGCTRDQGQLDSKCDCDPAGISGPCDSGRCVCKPAVTGERCDRCRPRDYHLDRANPEGCTQCFCYGHSASCHASA

horse   201 DYSVHKIISAFHQDVDGWKAVQRNGSPAKLQWSQRHRDIFSSARRSDPVYFVAPAKFLGNQQVSYGQSLSFDYRVDRGGRHPSAHDVILEGAGLRITAPL
man     201 EYSVHKITSTFHQDVDGWKAVQRNGSPAKLQWSQRHQDVFSSAQRLDPVYFVAPAKFLGNQQVSYGQSLSFDYRVDRGGRHPSAHDVILEGAGLRITAPL
mouse   201 DFSVHKITSTFSQDVDGWKAVQRNGAPAKLHWSQRHRDVFSSARRSDPVYFVAPAKFLGNQQVSYGQSLSFDYRVDRGGRQPSAYDVILEGAGLQIRAPL

horse   301 MPLSKTLPCGITKTYTFRLNEHPSSNWSPQLSYFEYRRLLRNLTALR-IRATYGEYSTGYIDNVTLISARPVSGAPAPWVEQCVCPVGYKGQFCQDCASG
man     301 MPLGKTLPCGLTKTYTFRLNEHPSNNWSPQLSYFEYRRLLRNLTALR-IRATYGEYSTGYIDNVTLISARPVSGAPAPWVEQCICPVGYKGQFCQDCASG
mouse   301 MAPGKTLPCGITKTYTFRLNEHPSSHWSPQLSYFEYRRLLRNLTALLMIRATYGEYSTGYIDNVTLVSARPVLGAPAPWVERCVCLLGYKGQFCQECASG

horse   400 YKRDSARLGPFGTCIPCNCQGGGACDPDTGDCYSGDENPDIPECADCPIGFYNDPQDPRSCKPCPCRNGFSCSVMPETEEVVCNNCPQGVTGARCELCAD
man     400 YKRDSARLGPFGTCIPCNCQGGGACDPDTGDCYSGDENPDI-ECADCPIGFYNDPHDPRSCKPCPCHNGFSCSVMPETEEVVCNNCPPGVTGARCELCAD
mouse   401 YKRDSARLGAFGACVPCNCQGEGACDPDTGDCYSGDENPDI-ECADCPIGFYNDPHDPRSCKPCPCHNGFSCSVMPETEEVVCNNCPPGVTGARCELCAD

horse   500 GYFGDPFGERGPVRPCQPCQCNNNVDPSASGNCDRLTGRCLKCIHNTAGVHCDQCKAGYYGDPLAPNPADKCRACNCNPVGSEPVECRSDGSCVCKPGFG
man     499 GYFGDPFGEHGPVRPCQPCQCNNNVDPSASGNCDRLTGRCLKCIHNTAGIYCDQCKAGYFGDPLAPNPADKCRACNCNPMGSEPVGCRSDGTCVCKPGFG
mouse   500 GFFGDPFGEHGPVRPCQRCQCNNNVDPNASGNCDQLTGRCLKCIYNTAGVYCDQCKAGYFGDPLAPNPADKCRACNCSPMGAEPGECRGDGSCVCKPGFG

horse   600 GLSCEHAALTSCPACYNQVKVQMDQFMQQLQILEALISKAQGG---AVPNAELEGRMQQAEQALRDILREAQISQDAVRSFNLRVAKARTQENSYRDRLD
man     599 GPNCEHGAFS-CPACYNQVKIQMDQFMQQLQRMEALISKAQGGDG-VVPDTELEGRMQQAEQALQDILRDAQISEGASRSLGLQLAKVRSQENSYQSRLD
mouse   600 AFNCDHAALTSCPACYNQVKIQMDQFTQQLQSLEALVSKAQGGGGGGTVPVQLEGRIEQAEQALQDILGEAQISEGAMRAVAVRLAKARSQENDYKTRLD

horse   697 DLKMTVERVRALGSQYQNQVQDTRRLITQMRLSLEESEASLQNTNIPPSEHYVGPNGFKSLAQEATRLADSHVQSASNMEQLAKETQEYSKELMSLVREA
man     697 DLKMTVERVRALGSQYQNRVRDTHRLITQMQLSLAESEASLGNTNIPASDHYVGPNGFKSLAQEATRLAESHVESASNMEQLTRETEDYSKQALSLVRKA
mouse   700 DLKMTAERIRALGSQHQNRVQDTSRLISQMRLSLAGSEALLENTNIHSSEHYVGPNDFKSLAQEATRKADSHAESANAMKQLARETEDYSKQALSLARKL

horse   797 LQE--GGGSGSLDGAVVQRLVGKLQKTKSLAQELSREATQTDMEADRSYQHSLHLLNSVSQIQGVNDQSLQVEAKR-LRQKADSLSNRVTKHMDEFKHVQ
man     797 LHEGVGSGSGSPDGAVVQGLVEKLEKTKSLAQQLTREATQAEIEADRSYQHSLRLLDSVSRLQGVSDQSFQVEEAKRIKQKADSLSTLVTRHMDEFKRTQ
mouse   800 LSG--GGGSGSWDSSVVQGLMGKLEKTKSLSQQLSLEGTQADIEADRSYQHSLRLLDSASQLQGVSDLSFQVEAKR-IRQKADSLSNLVTRQTDAFTRVR

horse   894 SNLGNWEEETRQLLQNGKNGRQTSDQLLSRANLAKSRAQEALSMGNATFYEVENILKNLREFDLQVGDKRAEAEEAMKRLSYISQKVAGASDKTKQAEAA
man     897 KNLGNWKEEAQQLLQNGKSGREKSDQLLSRANLAKSRAQEALSMGNATFYEVESILKNLREFDLQVDNRKAEAEEAMKRLSYISQKVSDASDKTQQAERA
mouse   897 NNLGNWEKETRQLLQTGKDRRQTSDQLLSRANLAKNRAQEALSMGNATFYEVENILKNLREFDLQVEDRKAEAEEAMKRLSSISQKVADASDKTQQAETA

horse   994 LGSAAADAQRAKNAAREALEISGKIEQEIGGLNLEANVTADGALAMEKGLATLKSEMREVEGELSRKEQEFDMDMDAVQMVIAEAQRVENRAKNAGVTIQ
man     997 LGSAAADAQRAKNGAGEALEISSEIEQEIGSLNLEANVTADGALAMEKGLASLKSEMREVEGELERKELEFDTNMDAVQMVITEAQKVDTRAKNAGVTIQ
mouse   997 LGSATADTQRAKNAAREALEISSEIELEIGSLNLEANVTADGALAMEKGTATLKSEMREMI-ELARKELEFDTDKDTVQLVITEAQQADARATSAGVTIQ

horse  1094 DTLNTLDGILHLIDQPGSVDEERLILLEQKLFRAKTQINSQLRPLMSELEERAHRQKGHLRFLETSIDGILADVKNLENIRDNLPPGCYNTQALEQQ
man    1097 DTLNTLDGLLHLMDQPLSVDEEGLVLLEQKLSRAKTQINSQLRPMMSELEERARQQRGHLHLLETSIDGILADVKNLENIRDNLPPGCYNTQALEQQ
mouse  1096 DTLNTLDGILHLIDQPGSVDEEGMMLLEQGLFQAKTQINSRLRPLMSDLEERVRRQRNHLHLLETSIDGILADVKNLENIRDNLPPGCYNTQALEQQ
```

FIG. 4



Homozygous 1368insC

Heterozygous

Wild-type

FIG. 5

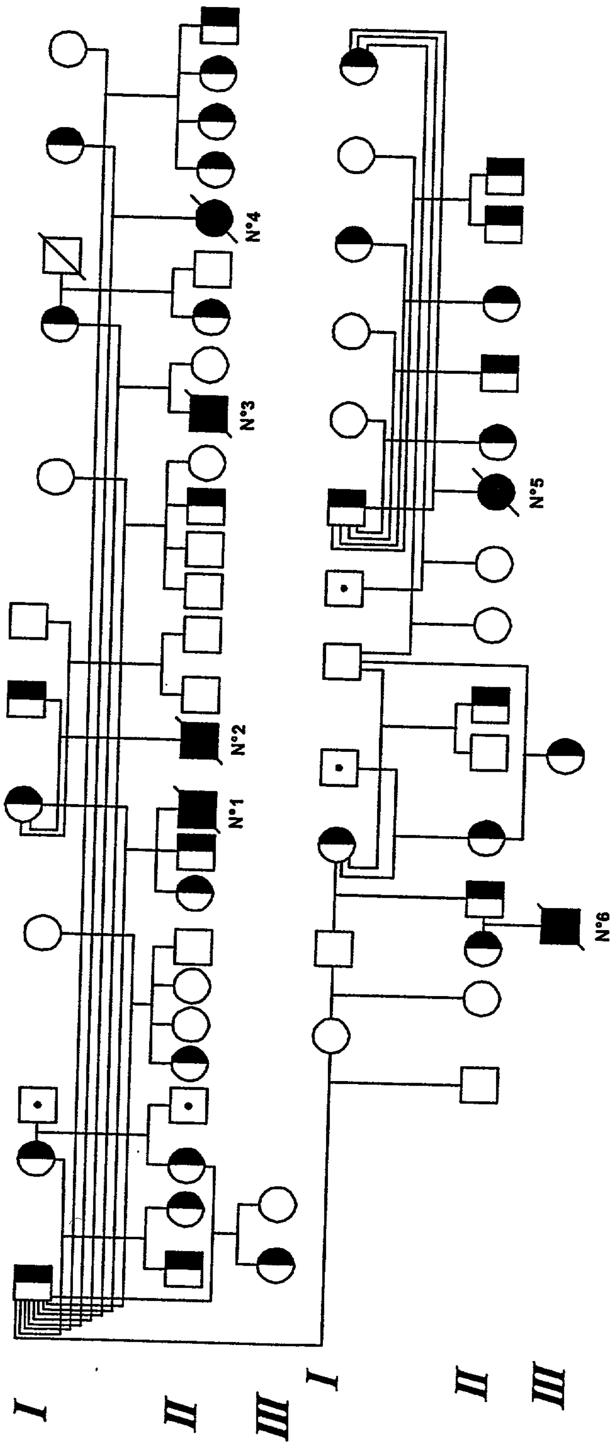


FIG. 6